(c) detecting morphogen inducible DNA binding to said transcription activating element by a cellular protein, said binding indicating the ability of said candidate compound to induce said morphogen mediated biological effect,

wherein step (c) occurs within approximately 2-12 hours of completing step (b),

Please add the following new claims:

43. The method of claim 1 wherein the morphogen is OP-1 or a related molecule.

44. The method of claim 2 wherein the protein has DNA also has binding properties of an AP-1 binding sequence.

REMARKS

Claims 1-42 are currently pending in this application, and claims 43 and 44 have been added by this Amendment. Antecedent support for claims 43 and 44 can be found throughout the application.

In the Official Action of March 29, 2001, claims 1-13, 15 and 30-36 were subject to an obviousness-type double patenting rejection over claims 1-10 of U.S. Patent No. 5,834,188. This rejection is based on a judicially created doctrine, and can be overcome by filing a terminal disclaimer.

Without conceding the appropriateness of this rejection, applicants would be prepared to submit a terminal disclaimer to obviate this rejection provided that the claims were otherwise in proper condition for allowance.

Claims 12 and 35 have been rejected under 35 U.S.C. 112, first paragraph, as not being enabled by the specification. In particular, the Examiner states that the specification provides no teaching or guidance that the claimed compounds will treat any disease.

Claims 12 and 35 have now been cancelled without prejudice. Accordingly, this ground of rejection has been effectively obviated.

Claims 11 and 30-34 have been rejected under 35 U.S.C. 112, first paragraph, as being indefinite. This ground of rejection is traversed.

Claims 30-33 have been amended to depend from elected claims. Claims 11 and 34 have been cancelled without prejudice. Accordingly, this ground of rejection has also been obviated.

Claims 1-3, 6, 9, 11, 13, 30-34 and 36 stand rejected under 35 U.S.C. 103(a) as obvious over the Foulkes et al. patent in view of the Lin et al publication. This ground of rejection is also traversed.

The Examiner states that Foulkes et al. disclose the essential elements of the method of claim 1, except that the reference does not teach the use of morphogen-responsive elements in the method. Foulkes et al. describe a method for contacting a cell with a molecule that transcriptionally modulates the expression of a gene of interest within the cell to effect the expression level of the protein encoded by the gene. Foukes et al. further state that the molecules (1) do not naturally occur within the cell, (2) specifically modulate expression of the gene of interest, and (3) bind to the DNA, RNA or protein through a domain which is not a ligand binding domain of a receptor naturally occurring within the cell.

The Examiner correctly notes that Foulkes fails to teach or suggest the use of morphogen responsive elements in the disclosed method. Accordingly, Foulkes et al. does not provide any mechanism for identifying candidate compounds that induce a morpohogen-mediated biological effect as required in the present invention.

The Lin et al reference has been cited in order to supply the deficiencies of the Foulkes et al. reference. Specifically, the Examiner states that Lin et al. discloses the use of promoters involved in morphogeneis, and that this feature can be combined with the method of Foulkes, et al..

Lin et al. discloses the characterization of the human plastin gene promoter. As part of this disclosure, the reference states that the plastin homologs found in yeast are required for actin organization and morphogenesis. However, Lin does not further describe the role of plastins or actin with respect to morphogenesis.

Applicants point out that the present claims have been amended to require that the compound identified according to the claimed method induces the formation of functional, differentiated mammalian tissue from uncommitted mammalian cells. The identification of compounds of this type is not disclosed in either reference. Moreover, the Lin et al. reference is silent as to the type of morphogenesis claimed in the present application, which involves the generation of differentiated mammalian cells from uncommitted cells. Accordingly, any

combination of Foulkes and Lin et al., each assuming such combination in proper, would still fail to teach or suggest the method claim in the present application.

The references cited as of interest have been reviewed, but are not deemed pertinent to the instant invention as presently claimed.

In view of the foregoing facts and reasons, this application is now believed to overcome the remaining rejections, and to otherwise be in proper condition for allowance. Accordingly, withdrawal of the rejections, and favorable action on this application is solicited. The Examiner is invited to contact the undersigned at the telephone number listed below if this is believed to facilitate allowance of this application.

Respectfully submitted,

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MARKED-UP CLAIMS

1. (Amended) A method for identifying a compound that induces [a morphogen-mediated biological effect] the formation of functional, differentiated mammalian tissue from uncommitted mammalian cells, the method comprising the steps of:

(a) providing a test cell comprising DNA defining

a morphogen-responsive transcription activating element, and, in operative association therewith, a reporter gene encoding a detectable gene product, said DNA, when present in a morphogen-responsive cell contacted with the morphogen, serving to induce transcription of said reporter gene;

(b) exposing said test cell to a candidate compound; and

(c) detecting expression of said detectable gene product, said expression indicating the ability of said candidate compound to induce the [said] morphogen mediated biological effect.

30. (Amended) A method of detecting a morphogen-mediated biological [affect,] effect, the method comprising the step of: detecting the DNA binding of [the protein of claim 26] a protein that induces the formation of functional, differentiated mammalian tissue from uncommitted mammalian cells, said protein having a polypeptide chain selected from the group consisting of (a) a morphogen-inducible DNA binding protein which can interact with nucleotides 699-711, 715-724, 699-731, 682-731, 703-724 or 682-761 of SEQ ID NO: 1; (b) species or allelic variants of (a); (c) truncated amino acid sequences of any of (a) and (b) inducible by a morphogen or analog thereof under native conditions, and (d) biosynthetic or recombinant variants of any of the above.

36. (Amended) A method for identifying a candidate compound that induces [a morphogen-mediated biological effect] the formation of functional, differentiated mammalian tissue from uncommitted mammalian cells, the method comprising the steps of:

(a) providing a test cell comprising DNA defining a morphogen-responsive transcription activating element, said DNA, when present in a morphogen

responsive cell contacted with the morphogen, serving to induce transcription of a reporter gene operatively associated with said transcription activating element;

(b) exposing said test cell to a candidate compound; and

(c) detecting morphogen inducible DNA binding to said transcription activating element by a cellular protein, said binding indicating the ability of said candidate compound to induce [said] the morphogen mediated biological effect,

wherein step (c) occurs within approximately 2-12 hours of completing step (b),